

WHAT IS CLAIMED IS:

Sub  
b2  
1 1. Use of a humanized antibody to alpha-4 integrin in  
2 the manufacture of a medicament for treating a disease  
3 selected from the group consisting of asthma, atherosclerosis,  
4 AIDS dementia, diabetes, inflammatory bowel disease,  
5 rheumatoid arthritis, transplant rejection, graft versus host  
6 disease, tumor metastasis, nephritis, atopic dermatitis,  
7 psoriasis, myocardial ischemia, and acute leukocyte mediated  
8 lung injury.

1 2. The use according to claim 1, wherein the disease is  
2 asthma.

1 3. The use according to claim 1, wherein the disease is  
2 atherosclerosis.

1 4. The use according to claim 1, wherein the disease is  
2 AIDS dementia.

1 5. The use according to claim 1, wherein the disease is  
2 diabetes.

1 6. The use according to claim 1, wherein the disease is  
2 inflammatory bowel disease.

1 7. The use according to claim 1, wherein the disease is  
2 rheumatoid arthritis.

1 8. The use according to claim 1, wherein the disease is  
2 transplant rejection.

1 9. The use according to claim 1, wherein the disease is  
2 graft versus host disease.

1 10. The use according to claim 1, wherein the disease is  
2 tumor metastasis.

09155739.091199  
B6T60"6E25T60

1 11. The use according to claim 1, wherein the disease is  
2 nephritis.

1 12. The use according to claim 1, wherein the disease is  
2 atopic dermatitis.

1 13. The use according to claim 1, wherein the disease is  
2 psoriasis.

1 14. The use according to claim 1, wherein the disease is  
2 myocardial ischemia.

1 15. The use according to claim 1, wherein the disease is  
2 acute leukocyte-mediated lung injury.

1 16. The use according to claim 17, wherein the disease  
2 is adult respiratory distress syndrome.

1 17. The use according to <sup>claim 1</sup> ~~any one of the preceding claims~~  
2 wherein the humanized antibody is a humanized form of the  
3 mouse 21.6 antibody.

1 18. The use according to claim 17, wherein the humanized  
2 antibody comprises a humanized heavy chain and a humanized  
3 light chain:

4 (1) the humanized light chain comprising three  
5 complementarity determining regions (CDR1, CDR2 and CDR3)  
6 having amino acid sequences from the corresponding  
7 complementarity determining regions of the mouse 21-6  
8 immunoglobulin light chain variable domain designated SEQ. ID.  
9 No. 2, and a variable region framework from a human kappa  
10 light chain variable region framework sequence except in at  
11 least one position selected from a first group consisting of  
12 L45, L49, L58 and L69, wherein the amino acid position is  
13 occupied by the same amino acid present in the equivalent  
14 position of the mouse 21-6 immunoglobulin light chain variable  
15 region framework; and

Sub B2  
"091198"  
66760



8 from the mouse 21.6 immunoglobulin at positions in the second  
9 group.

1 22. The use according to claim 21, wherein the humanized  
2 light chain variable region framework is identical to the RE1  
3 light chain variable region framework sequence except for the  
4 at least three positions from the first group and the three  
5 positions from the third group, and the heavy chain variable  
6 region framework is identical to the 21/28'CL heavy chain  
7 variable region framework sequence except for the at least  
8 five positions from the second group.

1 23. The use according to claim 22, wherein the at least  
2 three positions from the first group are positions L45, L58  
3 and L69, and at the least five positions from the second group  
4 are positions H27, H28, H29, H30 and H71.

1 24. The use according to claim 23, wherein the humanized  
2 light chain comprises complementarity determining regions that  
3 are identical to the corresponding complementarity determining  
4 regions of the mouse 21-6 heavy chain, and the humanized heavy  
5 chain comprises complementarity determining regions that are  
6 identical to the corresponding complementarity determining  
7 regions of the mouse 21-6 heavy chain, except that the CDR3  
8 region of the humanized heavy chain may or may not comprise a  
9 phenylalanine residue at position H98.

1 25. The use according to claim 24, wherein the amino  
2 acid sequence of the mature light chain variable region is the  
3 sequence designated La (SEQ. ID NO:7) in Fig. 6 and the amino  
4 acid sequence of the mature heavy chain variable region is Ha  
5 (SEQ. ID NO:11) in Fig 7.

1 26. The use according to claim 25, wherein the humanized  
2 antibody is a Fab fragment.

Sub  
P2  
0015739-091198

100  
64